24. (Unchanged From Prior Version) The method according to Claim 22, wherein said fluorescence dye is 2-methyl-4, 6-bis (4-N,N-dimethylaminophenyl) pyrylium salt.

25. (Unchanged From Prior Version) The method according to Claim 22, wherein said fluorescence dye is ethidium bromide.

26. (Unchanged From Prior Version) The method according to Claim 23, wherein said fluorescence dye is YOYO1.

REMARKS

This application has been reviewed in light of the Office Action dated August 28, 2002 (Paper No. 12). Claims 1-26 are in the application, of which Claims 1 and 20 are independent. Claims 1, 4, 5 and 20 have been amended to define more clearly what Applicants regard as their invention. Favorable reconsideration and further examination is respectfully requested.

Claims 1-26 were rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. In response, Claims 1, 4, 5 and 20 have been amended so as to improve clarity and to attend to the specific points raised in this rejection. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 1-7, 9, 11-14, 18, 20-22 and 25 were rejected under 35 U.S.C. § 103(a) over WO 87/06956 (Sutherland), in view of U.S. Patent 6,277,628 (Johann) and

U.S. Patent 6,268,131 (Kang). Claim 10 was rejected under 35 U.S.C. § 103(a) over WO 87/06956 (Sutherland), in view of U.S. Patent 6,277,628 (Johann), U.S. Patent 6,268,131 (Kang) and Japanese Patent 404330300 (Miyakoshi). In addition, Claims 15, 17, 19, 22-24 and 26 were rejected under 35 U.S.C. § 103(a) over WO 87/06956 (Sutherland), in view of U.S. Patent 6,277,628 (Johann), U.S. Patent 6,268,131 (Kang) and Nucleic Acid Research, 1995, Vol. 23(8), pg. 1445-1446 (Yamamoto). Applicants respectfully traverse and request reconsideration and withdrawal of the foregoing claim rejections.

The present claimed invention is directed to a method of dry detection/quantification of target nucleotide chains, in which a probe and target nucleotide chain are hybridized to form a hybrid in a solution, fluorescent dye is added to the hybrid, the hybrid and fluorescent dye are dried, and the fluorescence is measured. Additionally, one important feature is that the fluorescent dye is capable of emitting fluorescence in a dried state.

Although Sutherland may be deemed to teach the combining of fluorescent dye and a hybrid, the Examiner admits it does not teach the use of a fluorescent dye that emits fluorescence even after it is dry or the measurement of fluorescence after drying the hybrid and fluorescent dye. Johann is said to teach the drying of biomolecular probes and fluorescent dyes and detection of the fluorescent dye after drying.

The Examiner asserts that Kang provides motivation to combine Sutherland with Johann. Kang is said to teach that upon drying, the matrix DNA forms a uniform crystalline surface on the bottom of specified locations of the hybridized array. However, the drying in Kang was for purposes of mass spectrum analysis, which differs from the fluorescence detection methods of Sutherland and the present claimed invention. Mass

spectroscopy and fluorescence detection (e.g., fluorescence microscope) are different in kind. Each technique has its own different problems when in use. Kang fails to disclose detection of an oligonucleotide array through the use of fluorescent dye. Accordingly, Kang does not offer any motivation to combine Sutherland with Johann.

Moreover, certain problems associated with fluorescent dye detection in solutions was addressed in Sutherland using methods different from those of the claimed invention. The present claimed invention addresses specific problems of fluorescent dye detection in solution, such as quenching, through not only the step of measuring the fluorescence of the hybrid and fluorescent dye after drying, but also through the use of a fluorescent dye that emits fluorescence even in a dried state. Accordingly, none of the references, whether alone or in combination, teach the additional feature of the use of fluorescent dye that emits fluorescence while in a dried state.

Consequently, none of the references, whether considered alone or in combination, discloses or suggests the present claimed invention nor renders it unpatentable.

Accordingly, it is respectfully requested that the Claims be allowed and that the case be passed to issue.

Applicants' undersigned attorney may be reached in our Costa Mesa, California office at (714) 540-8700. All correspondence should continue to be directed to our below-listed address.

Respectfully submitted,

Attorney for Applicants

Registration No. 40,593

FITZPATRICK, CELLA, HARPER & SCINTO
30 Rockefeller Plaza
New York, New York 10112-2200
Facsimile: (212) 218-2200

CA_MAIN 55676 v 1

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE TO CLAIMS

1. (Amended) A method for dry detection/quantification of targeted nucleotide chains, comprising the steps of:

(1) [realizing a state in which] <u>forming</u> a hybrid (C) of a certain amount of a targeted nucleotide chain (A), [which is derived from a sample solution and subjected to detection or quantification], and a probe nucleotide chain (B), which has a base sequence complementary to a specific site of the base sequence of said targeted nucleotide chain, [is formed] on a solid-phase substrate by mutually reacting the two types of nucleotide chains with each other, and in which there exists a fluorescence dye (D), which acts on said hybrid (C), thereby emits fluorescence or increases its fluorescence intensity, and is capable of continuing to emit fluorescence even in [the] <u>a</u> dried state while acting on said hybrid;

(2) drying said hybrid (C) and said fluorescence dye (D) on said substrate; and

(3) measuring the fluorescence emitted from said fluorescence dye (D), as measuring means, after the drying operation.

4. (Amended) The method according to Claim 3, further comprising a step (1-0) of fixing said probe nucleotide chain (B) on the surface of said substrate before allowing [the same] <u>said probe nucleotide chain (B)</u> to act on said targeted nucleotide chain (A).

5. (Amended) The method according to Claim 3, further comprising a step (1-0') of fixing said targeted nucleotide chain (A) on the surface of said substrate before allowing [the same] <u>said</u>

targeted nucleotide chain (A) to act on said probe nucleotide chain (B).

20. (Amended) A method for dry detection/quantification of multi-stranded nucleotide chains, comprising the steps of:

(1) adding to a sample solution, which is subjected to detection/quantification of a multi-stranded nucleotide chain, a fluorescence dye having a fluorescence characteristic of emitting fluorescence or increasing its fluorescence intensity in the presence of a multi-stranded nucleotide chain and capable of maintaing the fluorescence characteristic [even] in [the] a dried state;

(2) placing a known amount of said sample solution with said fluorescence dye added thereto on a clean [observation] substrate so as to dry the sample solution [same]; and

(3) measuring the fluorescence emitted from the dried sample and detecting/quantifying said multi-stranded nucleotide chain in said sample solution based on [the] obtained measured values.